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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/496,041 02/02/00 TAKANO

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EXAMINER

KERR, K

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

09/25/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

| | | |
|-----------------|---------------|--|
| Application No. | Applicant(s) | |
| 09/496,041 | TAKANO ET AL. | |
| Examiner | Art Unit | |
| Kathleen M Kerr | 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on ____.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-8 and 20 is/are pending in the application.

4a) Of the above claim(s) ____ is/are withdrawn from consideration.

5) Claim(s) ____ is/are allowed.

6) Claim(s) 1-8 and 20 is/are rejected.

7) Claim(s) ____ is/are objected to.

8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on ____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. ____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the first Office action on the merits (Paper No. 8 mailed on April 10, 2001), an amendment was filed on July 16, 2001. Said action rejected all claims, Claims 1-8 that had been considered; the remaining pending claims, Claims 9-19, were withdrawn from consideration as non-elected inventions. Applicants' newly filed amendment canceled Claims 9-19, amended Claims 1, 3, 4, and 8, and added new Claim 20. Newly added Claim 20 is drawn to the elected invention.

Claims 1-8 and 20 are pending in the instant application and will be examined herein.

Election

2. Applicants' affirmation of the telephone election without traverse of Group I, original Claims 1-8, in Paper No. 9 is acknowledged. As noted above, new Claim 20 is drawn to the elected invention. Thus, Claims 1-8 and 20 will be examined herein.

Priority

3. As previously noted, receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. The priority claim in the instant application is based on a foreign language priority document for which no translation has been provided. Thus, for the purposes of prior art, the U.S. filing date of February 2, 2000 is considered the effective filing date.

Information Disclosure Statement

4. As previously noted, three (3) information disclosure statements have been filed in the instant application on February 2, 2000, June 13, 2000, and August 23, 2000; all three IDSs have been considered. Since no relevance can be cited for EP 023716, this reference has not been considered.

Drawings

5. As previously noted, the drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Sequence Compliance

6. With Applicants' statement under 37 C.F.R. § 1.821, the instant application is in full compliance with the sequence rules.

Withdrawn - Objections to the Specification

7. Previous objection to the specification for having an incomplete Abstract is withdrawn by virtue of Applicants' amendment to the Abstract.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

8. Previous rejection of Claims 1-8 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing the terms "carrying" and "introduced" is withdrawn by virtue of Applicants' amendments.
9. Previous rejection of Claim 8 under 35 U.S.C. § 112, second paragraph, as being indefinite for the redundant terms "acetic acid" and "acetate" is withdrawn. Applicants argue that acetic acid and acetate are distinct compounds since acetate is a salt of acetic acid. Since this is, in fact, the case (see enclosed definitions), the Examiner has dropped the rejection. However, it is noted that in the practice of the claimed method when acetic acid is used, one of ordinary skill in the art would also use a buffering system to achieve the proper pH for microorganism growth; such a buffering system would alter the "true" compound of acetic acid to its salt that is acetate.
10. Previous rejection of Claims 7-8 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn. Applicants' arguments have been fully considered and are deemed persuasive by virtue of the citations in the specification.

Maintained - Claim Rejections - 35 U.S.C. § 112

11. Previous rejection of Claims 1 and 5-8 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "precursor" in Claim 1 is maintained. Applicants' arguments have been fully considered but are not deemed persuasive.

Applicants argue that the specification has “shown that XMP, guanosine, inosine, and adenosine plainly function as examples of the precursors of purine nucleotides” (see Remarks page 7). The Examiner finds that the specification notes on page 11, lines 8 and 9, “precursors of purine nucleotides include XMP, guanosine, inosine.” The use of such examples implies a finite list, but does not expressly indicate such a limitation. Moreover, the purine nucleotide synthetic pathway is not identified in any finite way in the specification. Most biosynthetic pathways are integrated with other biosynthetic pathway and it is unclear if, for example, sugar biosynthesis is included as precursors. Applicants are invited to be their own lexicographers, but the definitions of their terms must be clear and not confused between art-defined terms and specification-defined terms.

12. Previous rejection of Claims 3-4 under 35 U.S.C. § 112, second paragraph, as being indefinite for the enzyme name “inosine-guanosine kinase or phosphatase” is maintained. Applicants have amended the claim to alter what was unclear as previously noted by the Examiner; however, the amendment also renders the claims confusing.

Applicants have amended the claim, but not according to the Examiner’s suggestion as they incorrectly noted. In fact, the amendment wholly changes the meaning of the claim. In the previous Office action, the Examiner had interpreted Claim 3 to limit the method of Claim 1 to a *single* enzyme that is inosine-guanosine kinase since the Examiner noted that “the claim language is attempting to read on the forward and backward reaction of kinases; this is clear from the enzyme name ---inosine-guanosine kinase--- without the term “phosphatase”. Inosine-guanosine kinase is also known as inosine kinase (E.C. 2.7.1.73 as enclosed) that converts inosine to IMP at the expense of ATP. This enzyme is specific for its substrate, inosine.

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A phosphatase-like reaction is the reverse reaction. However, an acid phosphatase reaction (E.C. 3.1.3.2 as enclosed) is a wholly different, nonspecific reaction that can dephosphorylate *various* orthophosphate monoesters, such as IMP and GMP. While this meaning is wholly different from that which the Examiner had previously interpreted.

Claims 3 and 4 are rejected because it is unclear how an acid phosphatase (or any phosphatase) can catalyze the production of a nucleotide since a nucleotide must be phosphorylated (see attached definition).

Withdrawn - Claim Rejections - 35 U.S.C. § 102

13. Previous rejection of Claim 8 under 35 U.S.C. § 102(b) as being anticipated by Fujio *et al.* (IDS reference) is withdrawn by virtue of Applicants' amendment to the claims. The inclusion of the promoter limitation renders this rejection moot for Claim 8; a new rejection is set forth below based on Applicants' amendment.

Maintained - Claim Rejections - 35 U.S.C. § 102

14. Previous rejection of Claims 1, 2, 5, and 7 under 35 U.S.C. § 102(b) as being anticipated by Fujio *et al.* (IDS reference) is maintained. Applicants' arguments have been fully considered, but are not deemed persuasive.

Applicants argue that Fujio *et al.* need two microorganisms and two fermentors. The Examiner disagrees since, as previously noted:

"Fujio *et al.* teach a method of production of GMP using *E. coli* transformed with a gene for GMP synthetase (XMP aminase) under the control of the temperature-sensitive P_L promoter (see page 842, right column). *E. coli* inherently contain XMP, a precursor; and Fujio *et al.* teach their method as industrial production of GMP, thus inherently containing a recovery step." (see Paper No. 8, paragraph 17)

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Applicants argue that nucleotide production cannot be conducted efficiently in *E. coli* alone; however, this argument is moot since no limitation of *efficient* nucleotide production is found in the pending claims. Applicants also argue that Claim 1 defines elements including precursor accumulation and *then* gene induction which elements are not taught by Fujio *et al.* Again, no limitation of accumulation levels is required, and, therefore, Fujio *et al.* is sufficient to teach all the limitations of the instant claims as noted above. While the Examiner does not disagree with Applicants' implication that Fujio *et al.* does not teach all the aspects of the invention as presented in the specification, the Examiner cannot read the limitations of the specification into the claims.

15. Previous rejection of Claims 1 and 3-6 under 35 U.S.C. § 102(b) as being anticipated by Usuda *et al.* (EP 0816491) (IDS reference) is maintained. Applicants' arguments have been fully considered, but are not deemed persuasive.

Applicants argue that Usuda *et al.* and the present invention are "quite different". The Examiner disagrees. As previously noted:

"Usuda et al. teach methods of making IMP and GMP by transforming a host cell, for example *C. ammoniagenes*, with a gene encoding inosine-guanosine kinase (see Example 1)." (see Paper No. 8, paragraph 18)

As noted above, none of the implications discussed in Applicants' traversal of the above rejection are pertinent given the claim limitations.

Withdrawn - Claim Rejections - 35 U.S.C. § 103

16. Previous rejection of Claim 8 under 35 U.S.C. § 103(a) as being unpatentable over Usuda *et al.* in view of Katsumata *et al.* (US 5,439,822) is withdrawn. The inclusion of the promoter

limitation renders this rejection moot for Claim 8; a new rejection is set forth below based on Applicants' amendment.

Maintained - Claim Rejections - 35 U.S.C. § 103

17. Previous rejection of Claim 7 under 35 U.S.C. § 103(a) as being unpatentable over Usuda *et al.* in view of Katsumata *et al.* (US 5,439,822) is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that because Usuda *et al.* does not teach the limitations of the base claim and because Katsumata *et al.* does not make up for these deficiencies, the rejection should be withdrawn. As noted above, Usuda *et al.* adequately anticipates the base claim, thus, Applicants' arguments are not persuasive.

NEW REJECTIONS

The following new grounds of objection/rejection are necessitated by Applicant's amendment.

New Objections to the Specification

18. The amendment filed on July 16, 2001 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

- a) On page 3, the paragraph starting on line 25, the word "acid" added before phosphatase.

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- b) On page 7, the paragraphs 3 and 4 starting on line 11, the word "acid" added before phosphatase in both paragraphs.
- c) On page 8, the paragraphs 15 and 16 starting on line 21, the word "acid" added before phosphatase in both paragraphs.
- d) On page 11, the paragraph starting on line 31, the word "acid" added before phosphatase.
- e) On page 12, the paragraph starting on line 12, the word "acid" added before phosphatase.
- f) On page 12, the paragraph starting on line 30, the word "acid" added before phosphatase.

While this particular subgenus of the genus of phosphatases may have been intended in the specification, it is neither expressly described or incorporated by reference and is, thus, new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

New Objections to the Claims

19. Claim 1 is objected to for not having the proper form; a final period is missing.

New Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claim 20 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "precursor" as maintained above for Claims 1 and 5-8.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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21. Claims 3 and 4 are rejected under 35 U.S.C. § 112, first paragraph, new matter, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a specific embodiment that includes using an "acid phosphatase" gene; no such genus of genes is described in the specification as originally filed.

New Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

22. Claims 8 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fujio *et al.* or Usuda *et al.* (EP 0816491) (IDS reference), either in view of Katsumata *et al.* (US 5,439,822). The instant claims are drawn to methods of making GMP and IMP in using an acetate-induction expression system of recombinant inosine-guanosine kinase.

Fujio *et al.* and Usuda *et al.* teach as described above. Neither reference teaches the use of the isocitrate lyase (ICL) promoter, a promoter useful for acetate induction.

Katsumata *et al.* teach the use of the ICL promoter for use in acetate-induction expression systems of recombinant genes (see column 1, lines 59-68).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Fujio *et al.* or Usuda *et al.* with Katsumata *et al.* because Katsumata *et al.* particularly describe the usefulness of the ICL promoter for efficient expression in coryneform and *E. coli* (see column 2, line 5-7 and column 3, line 9).

Summary of Pending Rejections

23. The following is a summary of the pending objections/rejections in the application:

- a) The specification is objected to for containing new matter in the form of acid phosphatase” (emphasis added).
- b) Claim 1 is objected to for not having the proper form; a final period is missing.
- c) Claims 1, 5-8, and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “precursor”.
- d) Claims 3-4 are rejected under 35 U.S.C. § 112, second paragraph, as being confusing due to the use of “inosine-guanosine kinase or acid phosphatase” (emphasis added).
- e) Claims 3 and 4 are rejected under 35 U.S.C. § 112, first paragraph, new matter, for the term “acid phosphatase” (emphasis added).
- f) Claims 1, 2, 5, and 7 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fujio *et al.* (IDS reference).
- g) Claims 1 and 3-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Usuda *et al.* (EP 0816491) (IDS reference).
- h) Claim 7 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Usuda *et al.* in view of Katsumata *et al.* (US 5,439,822).
- i) Claims 8 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fujio *et al.* or Usuda *et al.* (EP 0816491) (IDS reference), either in view of Katsumata *et al.* (US 5,439,822).

Conclusion

24. Claims 1-8 and 20 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-196.

KMK
September 20, 2001



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